In the Claims

The current status of the claims follows:

Claims 1 - 28 (Canceled)

Claim 29. (Currently Amended) A method for minimizing weight gain in a patient taking a psychotropic active compound comprising administering to said patient, who is in need of said compound and who also wishes to minimize weight gain, a safe and effective amount of a histamine H_2-receptor antagonist.

Claim 30. (Currently Amended) A method for minimizing weight gain in a patient taking a mood altering drug comprising administering to said patient, who is in need of said compound and who also wishes to minimize weight gain, a safe and effective amount of a histamine H_2-receptor antagonist.

Claim 31. (Currently Amended) A method for minimizing weight gain in a patient taking an unconventional antipsychotic drug comprising administering to said patient, who is in need of said compound and who also wishes to minimize weight gain, a safe and effective amount of a histamine H_2-receptor antagonist.

Claim 32. (Currently Amended) A method for minimizing weight gain in a patient taking a psychotropic active compound which is selected from a group consisting of clozapine, risperidone, quetiapine fumarate, divalproex, olanzapine and mirtazapine comprising administering to said patient, who is in need of such compound and who also wishes to minimize weight gain, a safe and

effective amount of a histamine H_2-receptor antagonist.

Claim 33. (Previously presented) The method of Claims 29, 30, 31 or 32 where the histamine H_2-receptor antagonist is selected from the group consisting of nizatidine, famotidine, cimetidine, and ranitidine.

Claim 34. (Previously presented) The process of Claim 29, 30, 31 or 32 wherein the histamine H_2-receptor antagonist is given separately from the psycho tropic drugs.

Claim 35. (Currently amended) A psycho tropically active controlled weight gain drug composition comprising a safe and effective amount of a psycho tropically active drug in combination with a safe and effective amount of a histamine H_2-receptor antagonist <u>for use by patients in need of said drug composition who also wish to minimize weight gain.</u>

Claim 36. (Currently amended) A mood altering controlled weight gain drug composition comprising of a safe and effective amount of mood altering drug in combination with a safe and effective amount of a histamine H_2-receptor antagonist <u>for use by patients in need of said drug composition who also wish to minimize weight gain.</u>

Claim 37. (Currently amended) An antipsychotic controlled weight gain drug composition comprising of a safe and effective amount of an antipsychotic drug in combination with a safe and effective amount of a histamine H_2-receptor antagonist <u>for use by</u>

patients in need of said drug composition who also wish to minimize weight gain.

Claim 38. (Currently amended) A psycho tropically active controlled weight gain drug composition comprising of a safe and effective amount of an psycho tropic active compound which is selected from the group consisting of olanzapine, clozapine, risperidone, quetiapine fumarate, divalproex, olanzapine and mirtazapine in composition with a safe and effective amount of a histamine H_2-receptor antagonist for use by patients in need of said drug composition who also wish to minimize weight gain.

Claim 39. (Previously presented) The composition of Claims 35, 36, 37 or 38 wherein the histamine H_2-receptor antagonist is selected from the group consisting of nizatidine, famotidine, cimetidine, and ranitidine.

BASIS FOR AMENDMENT

The applicant has discovered a method for the prevention and reversal of weight gain associated with the use of olanzapine and other antipsychotic or mood stabilizing drugs through the concomitant use of histamine H_2-receptor antagonists. The combination use of a psychotropic active drug with a histamine H_2-receptor antagonist not only effectively treats the mental illness, which has caused the prescription of the antipsychotic or mood stabilizing drug, but surprisingly results in the prevention or reversal of weight gain associated with the use of these antipsychotic or mood stabilizing drugs.

In order to emphasize the relationship between the use of these two types of drugs and the impact of utilization of this combination of drugs on weight loss, each of the independent claims of the application have been amended to positively claim that the method to prevent weight gain in patients taking psychotropic drugs is the administration of the claimed combination of drugs. This Amendment is contained in method Claims 29 - 32. Further, the particular drugs of choice, not only for the treatment of the mental illness, but also to minimize or reduce weight gain from taking of the psychotropic drugs, are also contained in amendments to independent Claims 35 - 38, which state that this combination of drugs is specifically "for use by patients in need of said drug composition who also wish to minimize weight gain."

These amendments were suggested by the Examiner in the Office Action dated April 6, 2004 in the first paragraph on the top of page 3. This amendment is also implied by the Examiner at various other places throughout the Office Action. Basis for this Amendment is present throughout the application, for example in the title: page 1, lines 9 - 16; page 2, lines 16 - 17; page 3, lines 2 - 3; page 15, lines 17 - page 16, line 2; and in the Abstract. Further, the Examiner accepts that this amended language is disclosed within the application by his suggestion for incorporation of this limitation into the claims at the top of page 3 of the Office Action.

No new subject matter is introduced by any of these amendments.

Analysis of Rejections.

Claims 29 - 32 and 34 were rejected as being anticipated by Deutsch, et. al. The applicant respectfully traverses this rejection.

The USPTO asserts that Deutsch, et. al. teach each of the required process steps. However, the Examiner acknowledges at the top of page 3 that "incorporation of a limitation to narrow the scope of the patients" should be sufficient to overcome this rejection. Accordingly, the applicant has amended the rejected claims in the manner suggested by the Examiner and asserts that said amendments overcome the rejection under 35 USC §102.

Rejection under 35 USC §103.

The USPTO further asserts that Claims 29 - 39 are unpatentable over Rosenberg in view of Deutsch, et. al. The applicant also respectfully traverses this rejection.

The applicant asserts that the amendment to the claims to emphasize that the process is useful in patients in need of psychotropic active compounds or mood altering drugs who also wish to minimize weight gain during the period of time in which they are taking the psychotropic active compound or mood altering drug overcomes this rejection. Claims 35 - 39 have also been amended to emphasize that the utilization of the histamine H_2-receptor antagonist in combination with the psychotropic active drug, mood

altering drug or antipsychotic drug is designed for utilization for patients in need of the active drug composition who also wish to minimize weight gain. This claim language emphasizing the use of these drugs in combination has been incorporated into all claims of the application. The applicant asserts that this amendment to the claims overcomes the rejection by the USPTO.

The USPTO asserts that Rosenberg teaches a process for making covered tablets, which may contain one or more pharmaceutically active ingredients. The USPTO asserts that this reference teaches that there is general knowledge that any group of drugs could be combined which could be "suitable for a therapeutic purpose." Further, the USPTO asserts that "there is ample suggestion to one of ordinary skill in the art to combine an antipsychotic and a histamine antagonist for at least the purpose taught in Deutsch, et. al."

The applicant respectfully asserts that the USPTO has failed to satisfy its burden to establish *prima facie* obviousness. To reject claims under 35 USC § 103, the USPTO is required to identify where in the cited references, i.e., Deutsch, et. al. and Rosenberg, there is a motivating suggestion to combine a psychotropic active compound, a mood altering drug or an unconventional antipsychotic drug with a histamine H_2-receptor antagonist specifically for a patient in need of said active compound "who wishes to minimize weight gain." Such motivation is

clearly not present in either reference. In fact, the Examiner inherently acknowledges that there is no statement in either reference that the combination of these drugs would result in a minimization of weight gain as required to prove *prima facie* obviousness.

In In re Jones, 958 Fed.2d 347, 21 USPQ2d 1941, 1944 (Fed. Cir. 1992), citing In re Lalu, 747 Fed2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir. 1984), the Court stated that "[t]he prior art must provide one of ordinary skill in the art the motivation to make the proposed... modification needed to arrive at the claim compound." The USPTO has failed to disclose any suggestion or motivation from either reference which would suggest the combination of a psychotropic, mood altering or antipsychotic drug to be utilized with a histamine H_2-receptor antagonist for a patient in need of the active drug who also wishes to minimize weight gain from taking that drug.

Moreover, the USPTO has failed to prove that the combination of these two types of drugs is a "desirable" modification to cause the minimization of weight gain. The "desirability" of the motivation must also be proved to establish *prima facie* obviousness.

> The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make modification obvious, unless the prior art suggested the desirability of the modification. In re Fritch, 922 Fed.2d 1260, 23 USPQ2d 1780, 1783-84 (Fed. Cir. 1992).

In addition, the USPTO has failed to show that the motivating suggestion to combine these two different types of drugs for patients in need of a mental illness drug, but who also wishes to minimize weight gain, is an "explicit" suggestion and not merely some vague reference to a possible modification.

> ...Invention can not be found obvious unless there was some explicit teaching or suggestion in art to motivate one of ordinary skill to combine elements so as to create same invention. Winner International Royalty Corp. vs. Wang, 48 USPQ2nd 1139, 1140 (D.C.D.C. 1998)

Clearly there is no teaching of a motivation within either of these references that it would be desirable to combine an effective mental illness drug with a histamine H_2-receptor to minimize weight gain, much less an explicit teaching of this result.

The USPTO asserts in support of its position that the disclosures contained in WO 92/00736, the inventor of which is Dr. Stoa-Birketvedt, provides this knowledge. In this reference Dr. Stoa-Birketvedt cites two patents from 1979 (Vivino and Ritter) which attempt to use a histamine H_2 antagonist as an aid in weight loss. She then states that there has not been any subsequent publications to support or confirm these suggestions as of 1990. "[T]here do not appear to have been any subsequent publications which have supported or confirmed these suggestions." Page 1, lines 27 - 29. This is a clear indication that these references failed to teach that these drugs were successful as weight loss agents as no one else pursued this concept.

In addition, the teaching of Dr. Stoa-Birketvedt requires a very restrictive use of cimetidine, requiring that it be used in combination with a viscous suspension agent, which is commercially known as "Tagagel," along with dietary fiber, low calorie intake (between 1500 and 1200 kcals), and moderate exercise. (Page 3, line 29 - page 4, line 12.) Clearly, even from a non-expert reading of this reference, it is unclear whether and to what extent the administration of the cimetidine or the dietary and exercise program resulted in the weight loss. The limitation on caloric intake and moderate exercise could have caused the weight loss by itself.

Further and of more importance, as stated in the attached affidavit from the applicant, who is an expert in the field, to his knowledge, there has been no clinically or commercial use of this process in the fourteen years since the filing of Dr. Stoa Birketvedt's application. Thus, there has clearly not been any acceptance of this concept.

This failure to accept the "limited" teaching of Dr. Stoa-Birketvedt is certainly surprising. As stated by the applicant in his attached affidavit, while there has certainly been a long felt need for addressing the problem of weight gain when taking antipsychotic or other mental illness drugs, the proposed solution advanced by the applicant has not be presented. In fact, the applicant states in his affidavit that there have been over two

hundred papers written in the medical literature from 1999 to 2004 dealing with some aspect of weight gain and/or other metabolic changes associated with the use of antipsychotics. In fact, recently the FDA compelled the manufacturers of all atypically antiphyschotics to place a warning on their package inserts about potential diabetes risks, which are a secondary result of weight gain. Thus, the applicant asserts that there has been no acceptance of his proposed method of prevention of weight gain without also the requirement of restricted caloric intake and increased exercise. Accordingly, the applicant asserts that there continues to be a long felt but unresolved need in the industry for treatment of this particular problem, which is resolved by the applicant's invention.

Finally, the applicant asserts on his affidavit that even when he submitted his proposed solution to the Journal of Clinical Psychiatry in 1999, it was rejected by a reviewer who stated "the conclusion of the authors that famotidine stabilizes the weight gain of these people is incorrect at best... the rational of adding an H_2 antagonist to a drug that authors are saying has substantial H_2 antagonism makes no sense." Accordingly, it is clear that to individuals skilled in the art, the concept proposed by the applicant in this invention was not accepted. The applicant's proposed solution is clearly surprising.